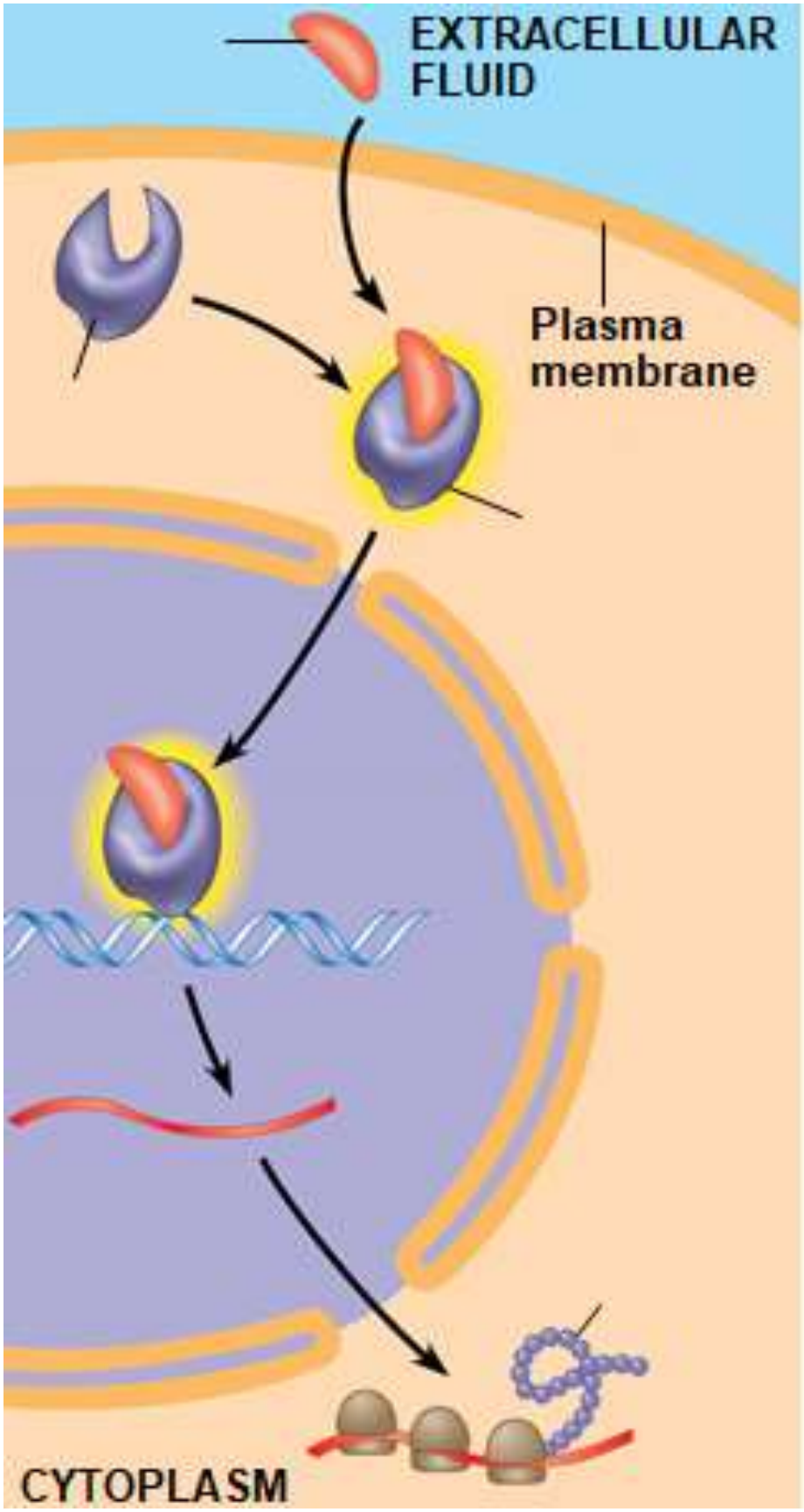
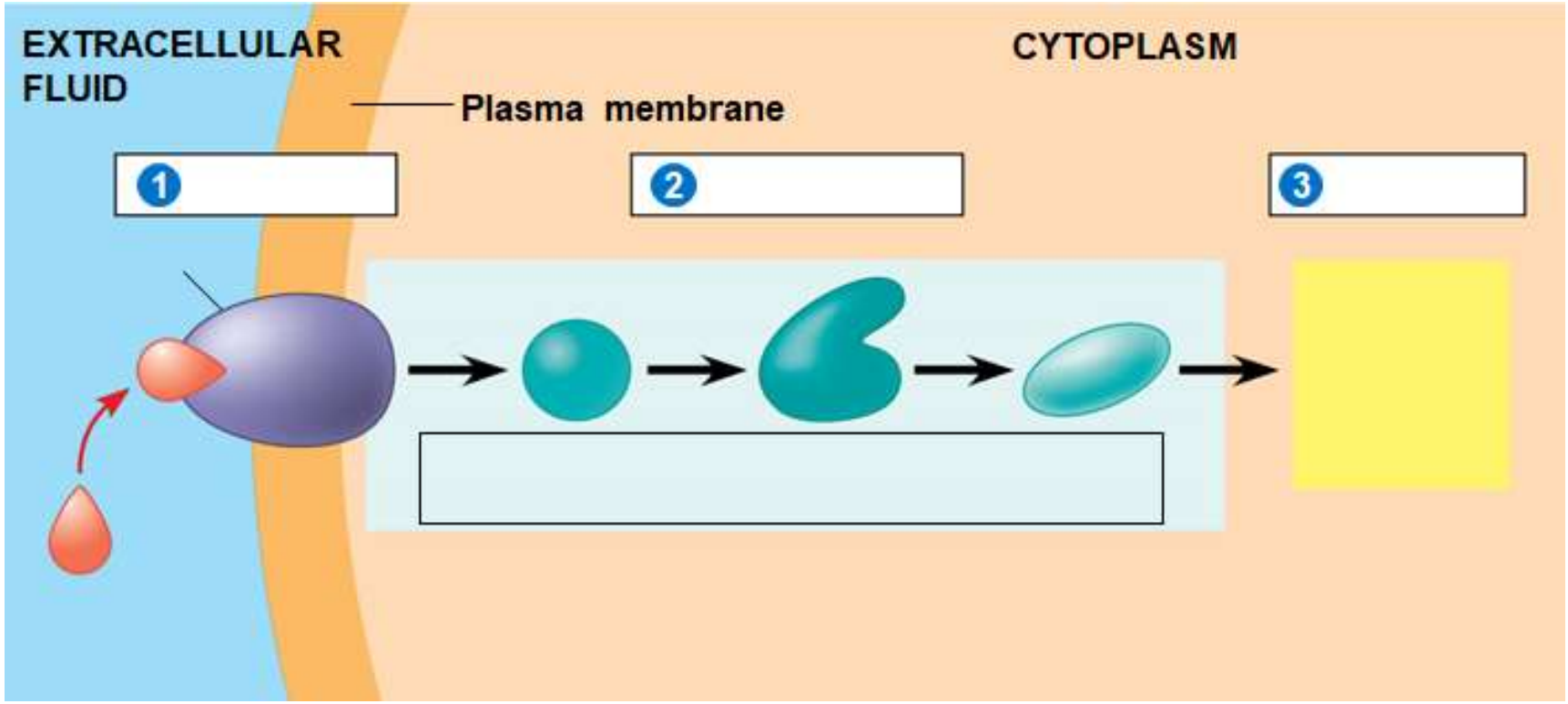
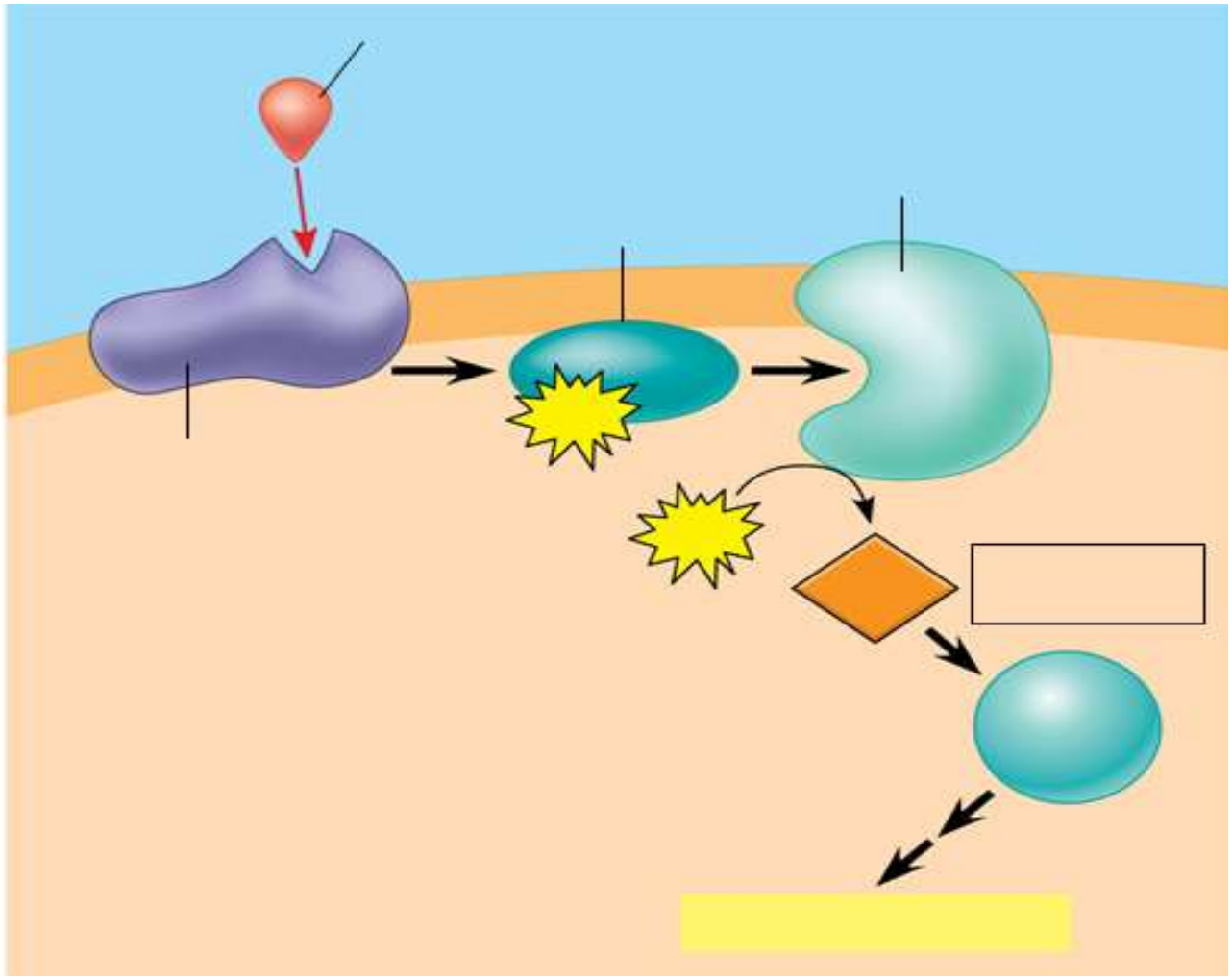
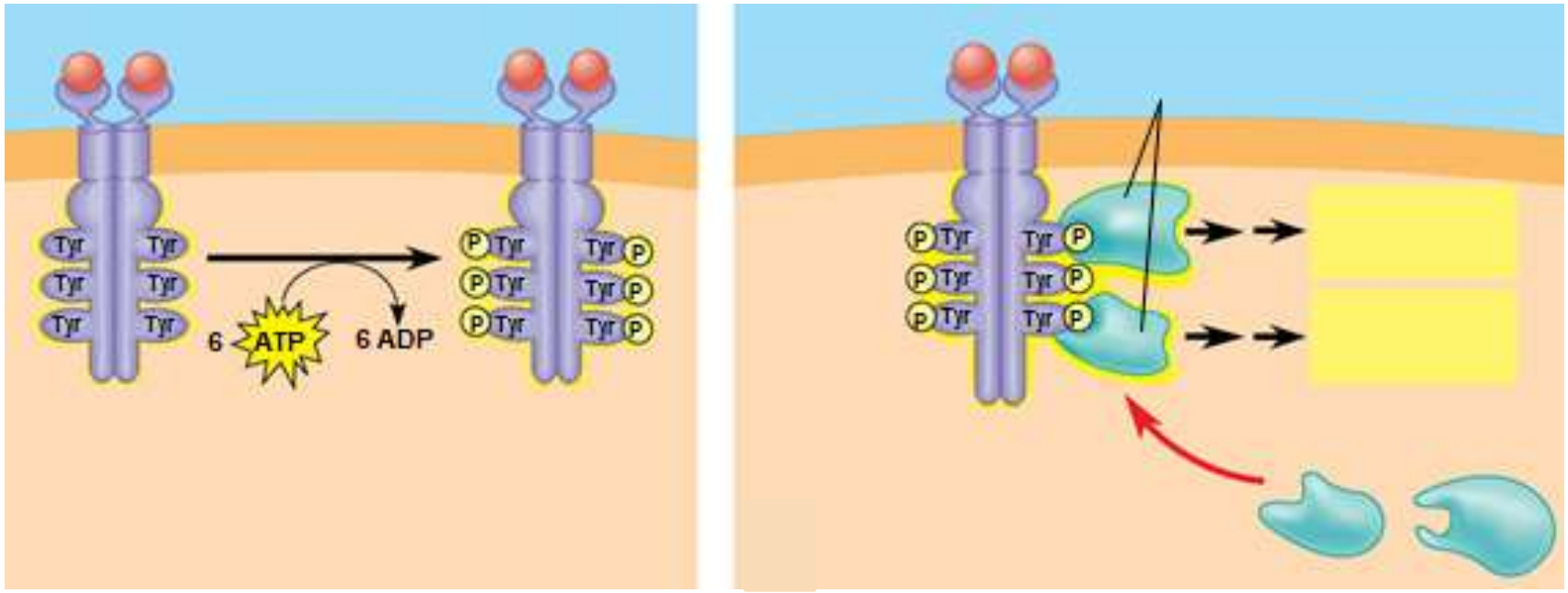

EXTRACELLULAR
FLUID
Plasma
membrane
CYTOPLASM


EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
1
2
3




Tyr
Tyr
Tyr
Tyr
Tyr
Tyr
6
ATP
6 ADP
P
Tyr
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P
P
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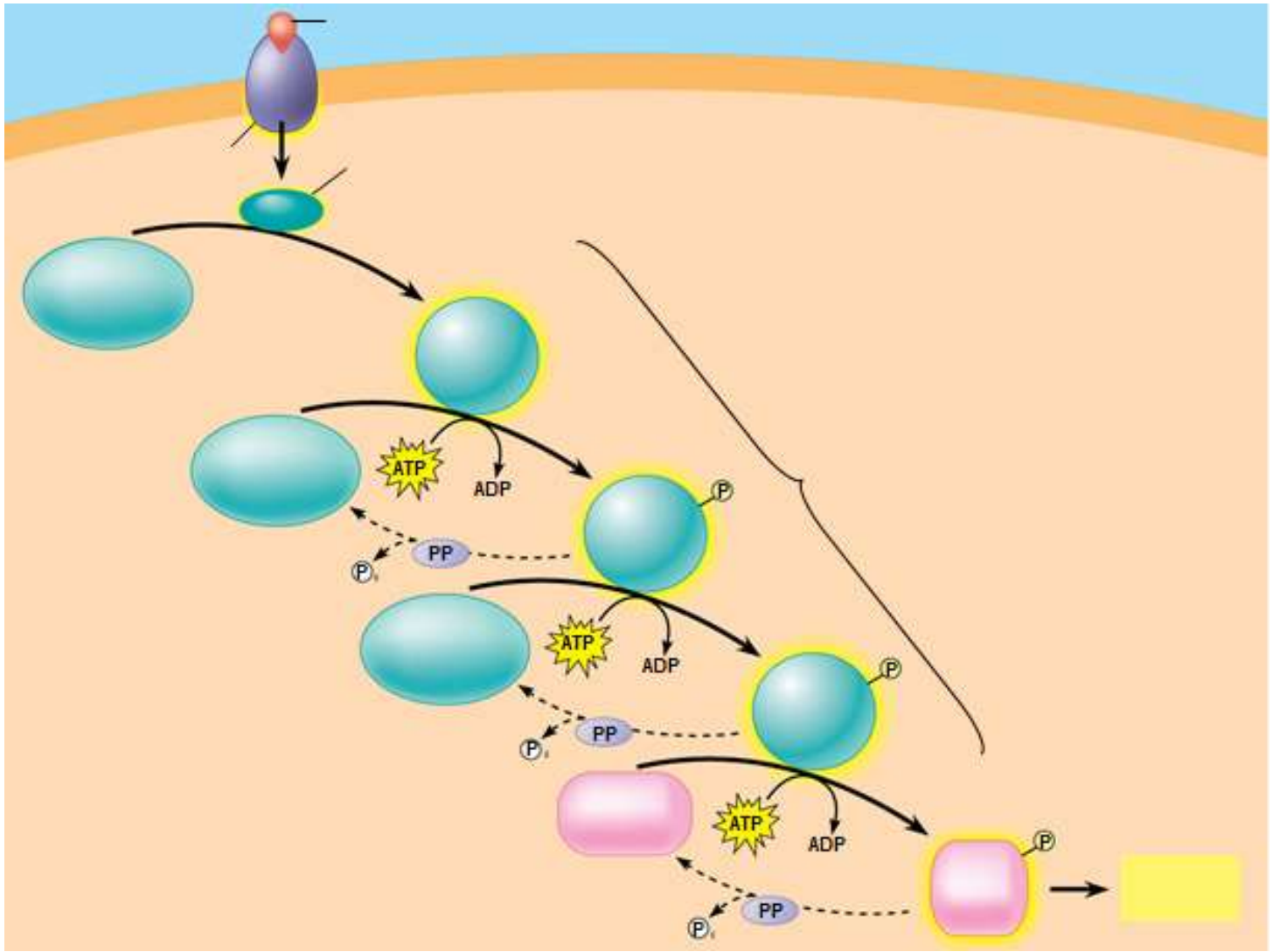
P
P
Tyr
Tyr
P


ATP
ADP
P
PP
P_i
ATP
ADP
P
PP
P_i
ATP
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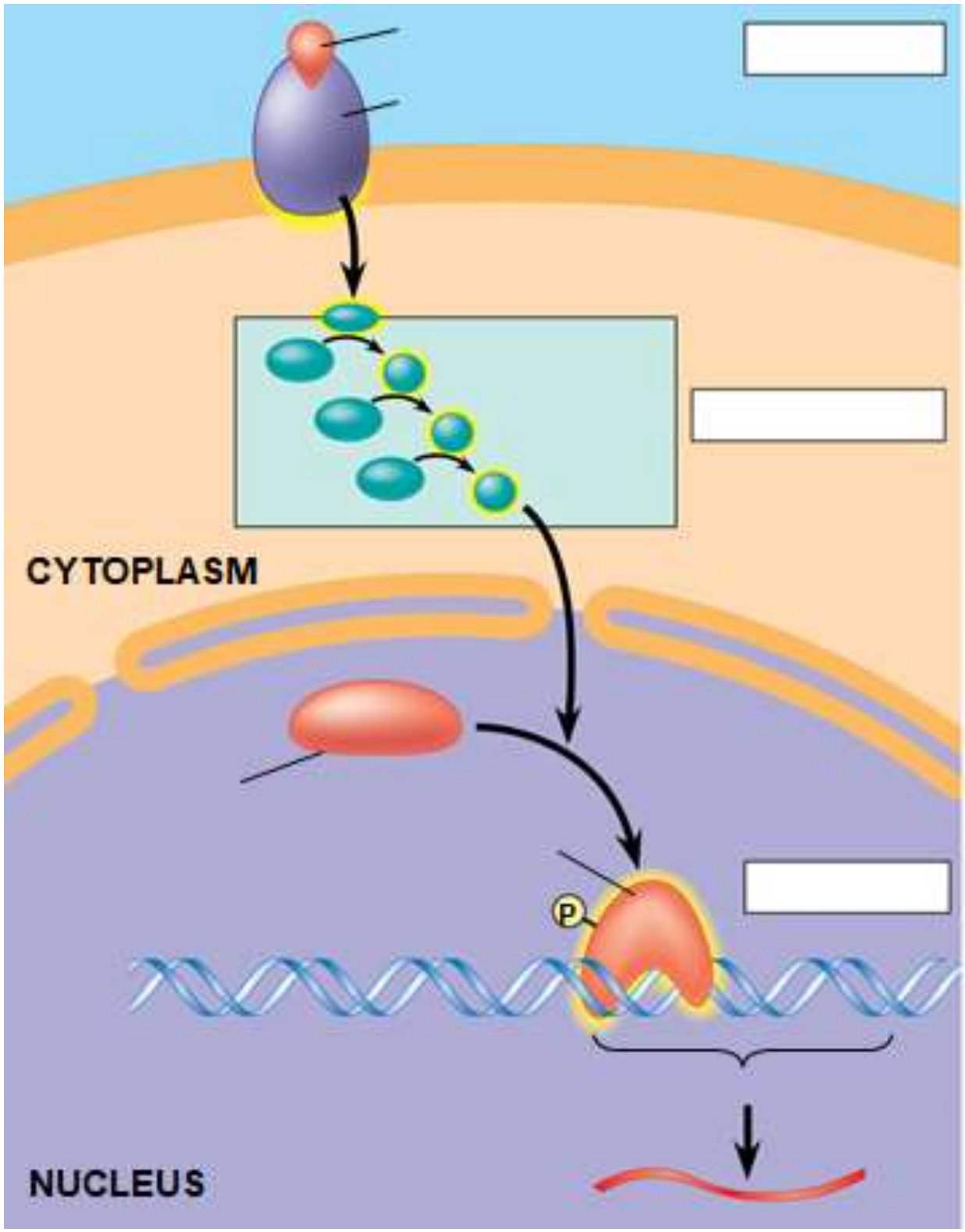
P
PP
P_i


CYTOPLASM
P
NUCLEUS

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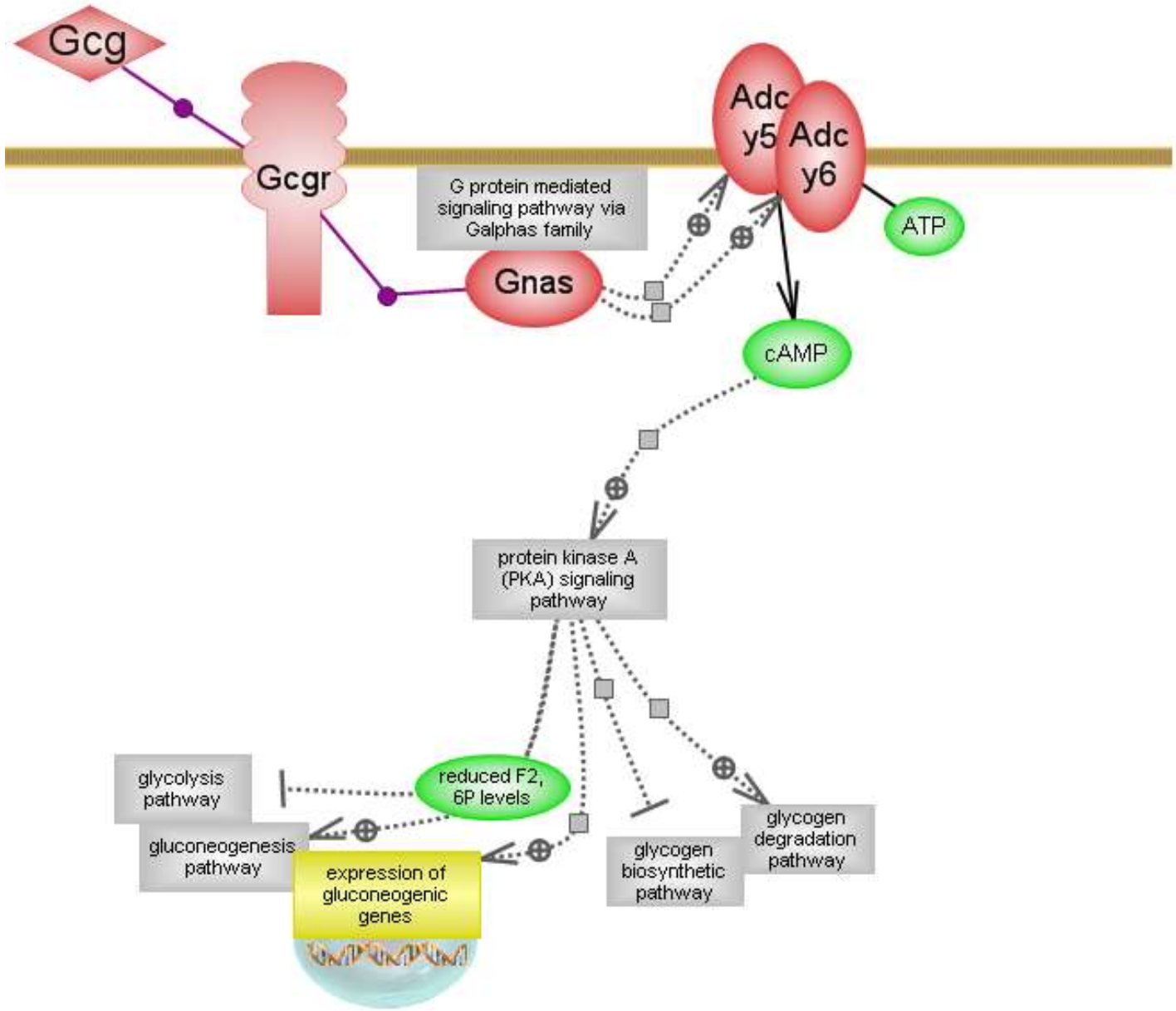
The protein hormone glucagon (Gcg) functions to increase the amount of glucose available in the blood. This function is the opposite of insulin which promotes absorption of blood glucose into body tissues. The signaling pathway follows a complex transduction pathway with numerous responses, but all with similar effects overall. The initiation step is when the Gcg ligand binds to the glucagon receptor (Gcgr), a transmembrane protein. The transduction pathway begins when Gcgr becomes activated and then it activates a G-protein (Gnas). Gnas activation causes it to bind ATP (not shown). Activated Gnas activates Adenylyl cyclase enzymes (Adcy5/Adcy6) that bind ATP and convert it into cAMP. cAMP activates the PKA signaling pathway which is a phosphorylation cascade. Each kinase enzyme will be energized by ATP and phosphorylate other relay proteins before being deactivated by phosphatase enzymes. This time between kinase activation and deactivation allows many relay molecules to be phosphorylated and amplify the signal many times. One response pathway is activating the glycogen degradation pathway: the PKA phosphorylations signal glycogen stored in cells to be broken down, making free glucose available to the blood. A second response pathway is inhibiting the glycogen biosynthetic pathway: the PKA phosphorylations signal glycogen polymerization enzymes to be inhibited, making free glucose stay available to the blood. A third response pathway is the gluconeogenic gene expression pathway: the PKA phosphorylations activate RNA polymerase enhancers, expressing genes that make enzymes for gluconeogenesis (synthesis of glucose from other biomolecules), making more glucose available for the blood. A final response pathway is the glycolysis inhibition pathway: the PKA phosphorylations activate inhibitors of a major glycolysis enzyme (F26P), assuring glycolysis can’t break down glucose, keeping the high blood glucose levels.


Gcg
Gcgr
G protein mediated signaling pathway via Galphas family
Gnas
Adc y5
Adc y6
ATP
cAMP
protein kinase A (PKA) signaling pathway
glycolysis pathway
reduced F2, 6P levels
gluconeogenesis pathway
expression of gluconeogenic genes
glycogen biosynthetic pathway
glycogen degradation pathway